International Color Manufacturers Association
(IACM)
1620 I Street, N.W.
Suite 925
Washington D.C. 20006

Tel. (202)-293-5800 Fax (202)-463-8998

Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue N.W.
Washington, D.C. 20460

October 23,2006

Dear Administrator:

On behalf of the International Color manufacturers Association (IACM), I wish to thank the Environmental Protection Agency (EPA) for their comments on the test plan and robust summaries on 2-naphthalenesulfonic acid, 6-hydroxy-5-[(2-methoxy-5-methyl-4-sulfophenyl)azo]-, disodium salt, FD&C Red No. 40 (CAS No. 25956-17-6).

The IACM serves is an industry consortium to coordinate testing activities for chemical substances under the Chemical Right-to-Know Program. Since 2000, the companies that are current members of IACM have supported the collection and review of available test data, development of test plans and robust summaries, and conducted additional testing.

Based on our initial recommendations and the peer-reviewed comments of the EPA, IACM is pleased to submit the following revised test plan and robust summaries for this substance. The revised test plan and robust summaries contain additional data on existing studies and the results of additional toxicity studies that are related to the questions and comments made by the EPA in its letter dated 04/16/2004. This letter contains responses to the specific comments made by the EPA. These responses taken together with the inclusion of new study data and other information constitute the key changes to the original test plan and robust summaries.

Based on these additional data, the IACM concludes that the current test plan and robust summaries for this food color is now complete. The experimental and model data for physiochemical properties, environmental fate, ecotoxicity, and human health endpoints are consistent and provide a comprehensive basis upon which to evaluate the hazard potential of FD&C Red No. 40. The U.S. Food and Drug

Administration has approved Red No. 40 for use in food (CFR 21, Part 74.340).
In an EPA letter dated 19 October 2001 concerning HPV-sponsored chemicals that are recognized as GRAS by the Food and Drug Administration, it was pointed out that:

" It may well be, on the basis of experience gained over years of use, that most of the substances have little compelling evidence suggesting that testing is needed in the context of the HPV Challenge Program. Nonetheless, while this line of reasoning could have been used to support the recommendation not to test the substances in this category, the information was only provided as background; few examples, and no actual data, were cited."

Without prior guidance from EPA, the International Color Manufacturers Association felt responsible to report endpoint data for this substance. Most of these data have already been provided to the US Food and Drug Administration during their evaluation of Red No. 40 as a food additive.

Based on the long history of use of Red No. 40 as a food additive, the hazard assessments performed by the US FDA, and the current regulatory status for the addition of this substance to the food supply, there is no compelling evidence that this substance should be further tested for physiochemical properties and human health endpoints in the EPA Chemical "Right to Know" Program. We do, however, maintain that data on the environmental fate and ecotoxicity are relevant to the HPV Challenge program. In this context, we have sponsored the collection of additional ecotoxicity data to provide a robust database on ecotoxicity endpoints. We consider that the test plan and robust summaries for Red No. 40 are final and have no plans to provide additional data. The EPA comprehensive comments provided the necessary guidance to complete the test plan for this category. The collaboration between the IACM and the Environmental Protection Agency in the Chemical "Right to Know" Program has produced a hazard database that will be useful to the public for decades to come. Thank you for the opportunity to participate in such a program.

If you have any questions or comments concerning the contents of this letter, please feel free to contact me at any time (202-331-2325) or tadams@therobertsgroup.net.

Best regards,

Timothy B. Adams, Ph.D.

Technical Contact Person for IACM

EPA Comments on Chemical RTK HPV Challenge Submission:
6-Hydroxy-5-[(2-methoxy-5-methyl-4-sulfophenyl)azo]-2-naphthalenesulfonic acid, disodium salt

SUMMARY OF EPA COMMENTS

The sponsor, The International Association of Color Manufacturers, submitted a test plan and robust summaries to EPA for 6-hydroxy-5-[(2-methoxy-5-methyl-4-sulfophenyl)azo]-2-naphthalenesulfonic acid disodium salt, (FD&C Red No. 40, CAS No. 25956-17-6) dated November 21, 2003. EPA posted the submission on the ChemRTK HPV Challenge Website on December 17, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Analog justification. The analogs used for the ecological endpoints—2,2'-(1,2-ethenediyl)bis(5-amino)-benzenesulfonic acid and its disodium and dipotassium salts—are not appropriate because they are too dissimilar structurally.

2. Physicochemical Properties. The data for these endpoints are adequate for the purposes of the HPV Challenge Program.

3. Environmental Fate. The data for these endpoints are adequate for the purposes of the HPV Challenge Program. The submitter needs to add input values used in the fugacity model to the fugacity robust summary.

4. Health Effects. The data for these endpoints are adequate for the purposes of the HPV Challenge Program.

5. Ecological Effects. As stated above, the analogs used are not appropriate to satisfy these endpoints; furthermore, EPA does not recommend the use of ECOSAR for anionic dyes. EPA recommends acute toxicity testing for fish and invertebrates, but not for algae because of the shading effect (inhibition of photosynthesis) of this type of dye.

Response: Ecotoxicity studies for two structurally related azo naphthalene- and benzene-sulfonic acid colorants, each in two species of fish and one invertebrate have been included in the robust summaries. LC50s are in the range from 50 to >500 mg/L indicating a low order of acute toxicity to fish. The test plan has been revised to reflect these additional data for the azo colorants. It is noteworthy that the ecotoxicity data on stilbenesulfonic acid derivatives is consistent with that for the azo colorants and the model data calculated from the EPA ECOSAR model.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE 6-HYDROXY-5-[(2-METHOXY-5-METHYL-4-SULFOPHENYL)AZO]-2-NAPHTHALENESULFONIC ACID, DISODIUM SALT CHALLENGE SUBMISSION

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data for all endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data for all endpoints are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The data for all endpoints are adequate for the purposes of the HPV Challenge Program.

Ecological Effects (fish, invertebrates, and algae)

The analogs—2,2'-(1,2-ethenediyl)bis(5-amino)benzenesulfonic acid and its disodium and dipotassium salts— proposed to meet these endpoints are not appropriate because they bear insufficient structural resemblance to the sponsored chemical. For example, the proposed analog has different substituents such as amino groups, is not an azo compound, and lacks the phenolic group. In addition, EPA does not recommend the use of ECOSAR for anionic dyes. Therefore, the aquatic toxicity endpoints have not been adequately addressed. EPA recommends acute toxicity testing for fish and invertebrates. EPA is not recommending testing for algae because the well-known "shading effect" (toxicity due to physical inhibition of photosynthesis) of this type of dye is expected to interfere with observation of any chemical toxicity to green algae.

Response: As noted earlier, acute fish and invertebrate toxicity data have been added to the robust summaries and test plan. Similar to other azo naphthalene sulfonic acid derivatives that are very water soluble, these colorants show no significant toxicity to aquatic species.

Specific Comments on the Robust Summaries

Environmental Fate

Fugacity. The submitter needs to add the input values used in the model to its fugacity robust summary.

Response: The input values have been added to the appropriate robust summary.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.